REMARKS

Claims 1-35 and 41-98 are pending. Consideration of the amendments and arguments presented on December 31, 2001 are respectfully requested.

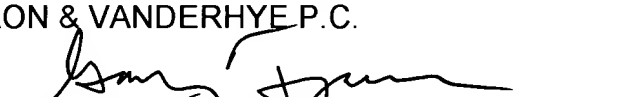
The amendments are supported by the original disclosure and, thus, no new matter has been added. If the Examiner should disagree, however, he is respectfully requested to point out the challenged limitation with particularity in the next Action so support may be cited in response.

In particular, in view of the amendment of December 31, 2001 that distinguishes the claimed invention over the prior art, Applicants have restored the original scope of the claims to include any adjuvant. The limitation that an antigen of the formulation is "at least partially purified" is supported by page 6, line 9, of the specification. Different types of adjuvants are described on page 15, lines 21-34, and page 18, lines 26-35, of the specification. Claims 73-75 and 84-86 are supported by page 16, lines 12-17 and 26-33, of the specification. The other new claims are similar to those already pending in this application.

Having fully responded to all of the pending objection and rejections of the Office Action (Paper No. 18), Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

Gary R. Tanigawa
Reg. No. 43,180

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

APPENDIX

MARKED-UP VERSION TO SHOW CHANGES

IN THE TITLE

The title is amended as follows: ADJUVANT [ADP-RIBOSYLATING EXOTOXIN USED] FOR TRANSCUTANEOUS IMMUNIZATION

IN THE CLAIMS

The claims are amended as follows.

1. (3 x Amended) A method of inducing an immune response comprising:

(a) applying a formulation to intact skin of an organism, wherein the formulation comprises (i) at least one antigen which is derived from a pathogen and (ii) at least one adjuvant [comprising an ADP-ribosylating exotoxin or derivative thereof having adjuvant activity], and an effective amount of the antigen which is not encapsulated induces the immune response;

(b) activating a Langerhans cell with the at least one adjuvant; and

(c) presenting the at least one antigen or epitope thereof on a cell surface of the Langerhans cell to a lymphocyte, thereby inducing the immune response in the organism.

22. (3 x Amended) The method of claim 1, wherein at least one adjuvant [the ADP-ribosylating exotoxin] is pertussis toxin or a derivative thereof having adjuvant activity.

23. (3 x Amended) The method of claim 1, wherein at least one adjuvant [the ADP-ribosylating exotoxin] is cholera toxin (CT) or a derivative thereof having adjuvant activity.

24. (3 x Amended) The method of claim 1, wherein at least one adjuvant [the ADP-ribosylating exotoxin] is *E. coli* heat-labile enterotoxin (LT) or a derivative thereof having adjuvant activity.

25. (3 x Amended) The method of claim 1, wherein at least one adjuvant [the ADP-ribosylating exotoxin] is diphtheria toxin (DT) or a derivative thereof having adjuvant activity.

26. (2 x Amended) The method of claim 1, wherein at least one adjuvant [the ADP-ribosylating exotoxin] is *Pseudomonas* exotoxin A or a derivative thereof having adjuvant activity.

31. (2 x Amended) A method of inducing an immune response comprising:

(a) applying a formulation to intact skin of an organism, wherein the formulation comprises (i) at least one antigen which is derived from a pathogen and (ii) at least one adjuvant [ADP-ribosylating exotoxin or derivative thereof having adjuvant activity], and at least some antigen which is not encapsulated induces the immune response; and

(b) inducing the immune response in the organism without perforating the skin, wherein the immune response is specific for the antigen.

32. (3 x Amended) A method of inducing an immune response comprising:

(a) applying a formulation to intact skin of an organism, wherein the formulation comprises (i) at least one antigen which is derived from a pathogen and (ii) at least one adjuvant [ADP-ribosylating exotoxin or derivative thereof having adjuvant activity], and at least some antigen which is not encapsulated induces the immune response;

(b) activating an antigen presenting cell with the at least one adjuvant [ADP-ribosylating exotoxin or derivative therof]; and

(c) presenting the at least one antigen or epitope thereof on a cell surface of the antigen presenting cell to a lymphocyte, thereby inducing the immune response in the organism.

33. (2 x Amended) A method of inducing an immune response comprising:

(a) applying epicutaneously on an organism an effective amount of at least one antigen derived from a pathogen and which is not encapsulated,

(b) activating a Langerhans cell underlying the organism's skin with at least one adjuvant [ADP-ribosylating exotoxin or derivative thereof having adjuvant activity],

(c) signaling the Langerhans cell to migrate to a lymph node of the organism and mature into a dendritic cell therein, and

(d) presenting the at least one antigen or epitope thereof on a cell surface of the dendritic cell to a lymphocyte; thereby inducing the immune response in the organism, wherein the immune response is specific for the at least one antigen.

41. (Amended) The method of claim 31, wherein the formulation comprises an ADP-ribosylating exotoxin derivative which is less toxic but remains immunogenic.

42. (Amended) The method of claim 31, wherein the formulation comprises a genetically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

43. (Amended) The method of claim 31, wherein the formulation comprises a chemically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

44. (Amended) The method of claim 31, wherein the formulation comprises an ADP-ribosylating exotoxin B subunit.

45. (Amended) The method of claim 1, wherein the formulation is comprised of at least partially purified antigen molecules as chemical or recombinant conjugates.

46. (Amended) The method of claim 1, wherein the formulation is comprised of an at least partially purified [a single] molecule containing both antigen and adjuvant properties.

47. (Amended) The method of claim 1, wherein the formulation is comprised of at least some antigen molecules which are at least partially purified and lack adjuvant properties.

48. (Amended) The method of claim 1, wherein the antigen is at least partially purified and has a molecular weight greater than 800 daltons.

49. (Amended) The method of claim 1, wherein the antigen is at least partially purified and has a molecular weight greater than 1000 daltons.

50. (Amended) The method of claim 1, wherein the antigen is an at least partially purified [a] polypeptide of greater than 800 daltons molecular weight.

51. (Amended) The method of claim 1, wherein the antigen is an at least partially purified [a] polypeptide of greater than 1000 daltons molecular weight.

53. (Amended) A method of immunization comprising applying a formulation without lipid vesicles to intact skin of an organism, wherein the formulation is comprised of an effective amount of one or more at least partially purified ADP-ribosylating exotoxins or derivatives thereof having adjuvant activity.

69. (Amended) A method of immunization comprising hydrating intact skin of an organism; applying an effective amount of one or more adjuvants [ADP-ribosylating exotoxins or derivatives thereof having adjuvant activity] to the hydrated, intact skin [in the absence of lipid vesicles]; and separately administering one or more at least partially

purified antigens which are derived from one or more pathogens in the absence of lipid vesicles such that the organism is effectively immunized.

Claims 70-98 are added as new claims.